Counting choline: why this nutrient is important and how we can measure it

Choline is an important nutrient for the growth and sustenance of living things, from humans to bacteria. Cells covert choline into phosphocholine via the activity of the enzyme choline kinase, and a change of other enzyme mediated chemical reactions leads to the conversion of phosphocholine into cell membrane elements, in the case of human cells, and into cell wall elements, in the case of bacteria. Both cell walls and cell membranes separate the cell from its environment, and help mediate the transfer of nutrients and waste to and from the cell and its environment, respectively. Therefore, anything that might interfere in the normal construction of cell walls and cell membranes are detrimental to the normal functioning of cells, as the normal transfer of nutrients and waste can only happen with healthy cell walls and healthy cell membranes. In the case of bacteria, cell walls have an additional function: they give the cell a strong structure, that protects the cell from osmotic pressure, or the pressure that occurs as water tends to transfer into the cell from its surrounding environment. In the case of bacteria, anything that interferes with the normal construction of a cell wall can cause it to explode under osmotic pressure.

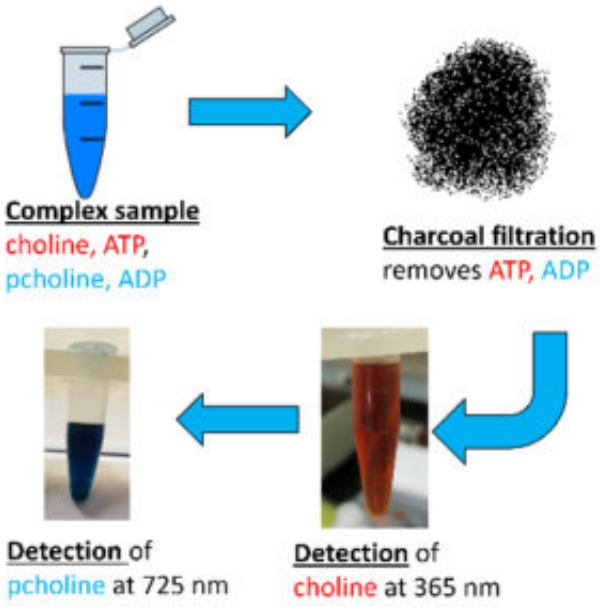

Fig. 1. Simplified schematic of our new colorimetric method for measuring choline and phosphocholine.

Since the initial step leading to the production of certain cell wall and cell membrane elements is the conversion of choline and phosphocholine via the enzyme choline kinase, measuring the

capacity of the cell to carry out this enzyme mediated reaction can tell something about the health of the cell. In addition, in certain cases, for example cancer cells or bacterial pathogens, we would like to block this initial chemical reaction in order to limit the growth of these disease causing cells. We can do this by designing drugs that specifically block the activity of choline kinase.

However, in order to follow whether or not the activity of choline kinase is efficiently being blocked, we need to measure how well the enzyme is working in the presence of the drug. That is, we need to be able to measure how much choline is being turned into phosphocholine over time in the presence of a drug. In order to know that, we measure both the amount of choline left, and the amount of phosphocholine that appears over time.

There are several techniques we can use to accomplish choline and phosphocholine measurements, but all currently either require huge capital investments and specialized knowledge (as in mass spectrometry) or require extra safety measures (as in radioactive labelling). Therefore, we have designed a colorimetric method that is both economical and relatively safe. This method is a twostep method that allows us to measure choline via the intensity of the color orange in a solution (Fig. 1) and measure phosphocholine via the intensity of the color blue in a solution. Each color is measured using a different wavelength in a device designed to measure color intensities: a spectrophotometer. Orange and blue are measured using the wavelength 365 nm and 725 nm, respectively. Using this technique, we can efficiently and economically test the efficacy of new drugs that target choline kinase, which opens the door to discover of new therapies for known diseases, from cancer to bacterial infections.

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